

Patent
Docket No: 54652US008

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Jerald K. RASMUSSEN and
Patrick L. COLEMAN

Group Art Unit: 1651

Continuation Application of Serial No. 09/240,829

Filed: February 1, 1999

Examiner: To Be Assigned

Serial No.: To Be Assigned

Filed: Herewith

For: WHOLE CELL SELECTION UTILIZING AZLACTONE-FUNCTIONAL SUPPORTS

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, DC 20231

Dear Sir:

Please enter the following Preliminary Amendment prior to examination of the application.

Please amend the application as follows:

IN THE SPECIFICATION

Please insert the following paragraph at the beginning of the specification.

This application is a continuation of co-pending U.S. Patent Application Serial No. 09/240,829, filed February 1, 1999.

Please substitute the following replacement paragraph for the paragraph beginning at page 7, line 12:

Other porous azlactone-functional supports are described in PCT Patent Publication WO 93/06925 (Rasmussen et al.) and U.S. Pat. No. 5,993,935 (Rasmussen et al.), issued November 30, 1999, incorporated herein by reference, in which azlactone-functional particles are incorporated into a continuous porous matrix such as fibrillated polytetrafluoroethylene membrane or a nonwoven web.

IN THE CLAIMS

Please cancel claims 1-11 without prejudice.

Please substitute amended claims 12 and 13 for pending claims 12 and 13. A version of the amended claims including markings to show the changes made is provided on a separate sheet.

12. (Amended) An interacted support, comprising:

- (a) an azlactone-functional support,
- (b) a biologically active substance covalently coupled to the support, and
- (c) whole cells interacting with said substance,

wherein the azlactone-functional support comprises one or more base polymer supports that have been prescreened and identified as exhibiting minimal nonspecific binding of the whole cells.

13. (Amended) The support of Claim 12, wherein the azlactone-functional support is a support having a surface comprising azlactone moieties, the support comprising a bead, a particulate, a membrane, a blended article, a graft copolymeric article, a woven web, a nonwoven web, a solid plastic particle, or any combination thereof.

Remarks

The present application is a continuation application of U.S. Ser. No. 09/240,829, filed February 1, 1999 (the '829 application). The claims of the present application were canceled in the '829 application by Applicants in an Amendment After Final, filed December 3, 2001.

Claims 1-17 are in the application.

Claims 1-11 have been canceled.

Claims 12 and 13 have been amended.

Claims 12-17 remain under consideration.

The specification has been amended to provide updated information identifying a reference cited in the text of the specification. No new matter is introduced by this amendment.

Claims 12 through 17 are submitted for examination on the merits. Claim 12, the lone independent claim, has been amended to be in the same form as claim 12 of the '829 application at the time it was canceled. Support for the amendment to claim 12 may be found throughout the specification, particularly from page 9, line 13 through page 10, line 6. Support for the amendment to claim 13 may be found throughout the application, particularly from page 6, line 15 through page 7, line 30.

At the time they were canceled from the '829 application, claims 12-17 stood rejected as being unpatentable over Rasmussen *et al.* (U.S. Pat. No. 5,993,935) in view of Rothschild *et al.* (U.S. Pat. No. 6,057,096) and Berenson *et al.* (U.S. Pat. No. 5,215,927), as stated in the Office Action mailed November 6, 2001.

The Office Action characterizes the disclosures of the cited references as follows. Rasmussen *et al.* discloses an azlactone-functional support containing a covalently bound ligand for use as an adsorbent to carry out affinity separations. Rothschild *et al.* discloses coupling cell adhesion molecules to a support to carry out separations of target cells. Berenson *et al.* discloses using immobilized avidin to isolate target cells that have been reacted with a biotinylated antibody to form a biotinylated cell complex. The Office Action states that it would have been obvious to use the bound ligand of Rasmussen *et al.* to separate target cells as suggested by Rothschild *et al.* and Berenson *et al.* The Office Action states that, with respect to claims 12-17, base supports prepared from materials recited in Rasmussen *et al.* will inherently have minimal binding for certain cells, and the claimed limitation that the base polymer supports are prescreened and identified as having minimal nonspecific binding of the whole cells does not exclude base supports used in Rasmussen *et al.*.

Applicants respectfully disagree with the position set forth in the Office Action. The interacted support claimed in claim 12 need not exclude the base polymers disclosed in Rasmussen *et al.* in order to be allowable. The interacted support of claim 12 is drawn to an interacted support including a base polymer that is a member of a species of base polymers prescreened and identified as having minimal nonspecific binding of the whole cells. The species of base polymers that serve to limit claim 12 is a species of base polymer selected from the broad genus of polymers disclosed in Rasmussen *et al.* A claim to a species within a genus is not rendered obvious and unpatentable by an earlier broad generic disclosure. *In re Baird*, 29 U.S.P.Q.2d 1550 (CAFC 1994).

In response to Applicants' argument set forth above, the Office Action points out that in *In re Baird*, the genus encompassed some 100 million different diphenols. The Office Action then asserts that in the present application, "the genus encompasses only about 15 different polymers as disclosed in col. 7, lines 31-39, of the '935 patent." The Office Action concludes that the genus of the present application "is much narrower" than the genus in *In re Baird* and, therefore, that one skilled in the art would have been able to select a polymer having minimal nonspecific binding for undesired cells.

Applicants respectfully disagree with the position set forth in the Office Action. Specifically, Applicants disagree with the characterization of the genus encompassed by the recitation of polymers in Rasmussen *et al.* Column 7, lines 28-39 of Rasmussen *et al.* reads:

The preferred materials useful to prepare nonwoven fibrous web for composite articles of the present invention include *polymers and copolymers* of monomers which form fibrous webs. Suitable polymers include polyalkylenes such as polyethylene and polypropylene, polyvinyl chloride, polyamides such as the various nylons, polystyrenes, polyarylsulfones, polyvinyl alcohol, polybutylene, ethyl vinyl acetate, polyacrylates such as polymethyl methacrylate, polycarbonate, cellulosics such as cellulose acetate butyrate, polyesters such as poly(ethylene terephthalate), polyimides, and polyurethanes such as polyether polyurethanes, *and combinations thereof.* (emphasis added)

Contrary to the assertion made in the Office Action, Rasmussen *et al.* recites a genus of preferred materials that encompasses a staggering number of different polymers. Rasmussen *et al.* recites about 14 different *classes* of materials that may be useful for preparing a nonwoven fibrous web. As applied to the present invention, each class of potentially useful materials includes at least dozens, in some cases hundreds, of different monomers that can be incorporated into the base polymer support of the present invention. Substituent groups distinguish monomers within a class and different substituents may contribute different chemistries to the resulting polymer, e.g., different nonspecific binding characteristics for a particular whole cell population. For example, *Polymer Handbook*, 4th ed. (1999), cites 239 different monomers in the class of materials referred to in Rasmussen *et al.* as polyacrylates (column 7, line 35), thereby identifying 239 different homopolymers that can be prepared solely from acrylate monomers. Thus, if one considers all of the classes of monomers recited in Rasmussen *et al.*, that reference recites materials that may be used to prepare many

hundreds of different homopolymers for use as base polymer supports for the present invention.

The materials recited in Rasmussen *et al.* include polymers and copolymers of combinations of monomers from one or more of the classes set forth above. That is, the building blocks for the polymers recited in Rasmussen *et al.* include monomers and oligomers, which are short polymers that are a combination of monomers, such as dimers, trimers, tetramers, and so on. Thus, polymers such as the polymers recited in Rasmussen *et al.* and the base polymer supports of the present invention may be prepared from combinations of, for example, two or more monomers and/or oligomers, each monomer or oligomer being a separate and distinguishable building block. Thus, the scope of the genus of materials recited in Rasmussen *et al.* is staggering and far exceeds the scope of the genus in *In re Baird*. For example, again considering only the class of 239 acrylates, the number of possible dimers that can be prepared from acrylate monomers is 239^2 , which is more than 57,000; the number of trimers that can be prepared is 239^3 , which is more than 13 million; the number of tetramers that can be prepared is 239^4 , which is more than three trillion; and so on. In other words, the number of building blocks that may be used to prepare the base polymer supports of the present invention, let alone all of the possible combinations of two, three, four or more of those building blocks, far exceeds the size of the genus in *In re Baird*, even when one only considers a single class of materials recited in Rasmussen *et al.*

The species of base polymer supports that limits claim 12 is a species in which the polymer used to prepare the support is selected from the broad genus of polymers recited in Rasmussen *et al.* Therefore, the rule of *In re Baird*, that a claim to a species within a genus is not rendered obvious and unpatentable by an earlier broad generic disclosure, applies. The species of base polymer supports that are prescreened and identified as exhibiting minimal nonspecific binding of whole cells is a nonobvious species within the broad genus of base polymer supports that can be made from the materials recited in Rasmussen *et al.*

Applicants further asserted in their response dated August 20, 2001 that the combination of Rasmussen *et al.*, Rothschild *et al.* and Berenson *et al.* is improper because one of skill in the art at the time the invention was made would have lacked motivation to combine those references as set forth in the rejection of the claims under 35 U.S.C. § 103. In order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally attributable to

one skilled in the art, to combine the reference teachings. MPEP § 2142. The Office Action asserts that such motivation is provided by Rothschild *et al.* and Berenson *et al.* because each describes using a cell adhesion molecule that binds only a desired target cell and not other cells. If a base polymer support binds cells other than target cells, then the objective of Rothschild *et al.* and Berenson *et al.* will be compromised. The Office Action argues that one skilled in the art, therefore, would have been motivated to select and prescreen for a base polymer support that provides minimal nonspecific binding of non-target cells.

Applicants submit that neither Rothschild *et al.* nor Berenson *et al.* provides the motivation as asserted in the Office Action. There is no specific motivation in Rothschild *et al.* or Berenson *et al.* for prescreening and selecting a base polymer support that exhibits minimal nonspecific binding of whole cells in order to minimize nonspecific binding of non-target cells.

In the absence of specific motivation from the references themselves, the motivation to combine the references must come from the knowledge generally attributable to one skilled in the art. Applicants submit that the Turkova reference accurately reflects the knowledge generally attributable to one skilled in the art at the time the invention was made. Applicants acknowledge that the Turkova reference does not assert that post-activation treatment of the support is the only way of reducing nonspecific binding. Rather, Applicants assert that one skilled in the art at the time the invention was made, without specific direction regarding how to minimize nonspecific binding of non-target cells, would have sought to minimize nonspecific binding of non-target cells by resorting to knowledge generally attributable to one skilled in the art, such as that described in Turkova or any other general reference documenting such generally attributable knowledge. No known reference teaches or suggests, either specifically or as knowledge generally attributable to one skilled in the art, minimizing nonspecific binding of non-target cells according to the present invention.

Any assertion that either Berenson *et al.* or Rothschild *et al.* provides motivation for minimizing nonspecific binding of non-target cells according to the present invention through knowledge generally attributable to one skilled in the art merely uses the Applicants' disclosure as a blueprint for constructing the Applicants' invention from elements found in the art, guided by hindsight derived from Applicants' disclosure. It is impermissible to use the Applicants' disclosure as a blueprint for combining prior art disclosures. In *Interconnect Planning Corp. v. Feil* (1985), the Federal Circuit directed that "The invention must be

viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time." 774 F.2d 1132, 1138, 227 USPQ 543, 547. The state of the art that existed at the time the present invention was made is reflected by the Turkova reference and would not have motivated one to minimize nonspecific binding of non-target cells by selecting a base polymer support that had been prescreened and selected to minimize such nonspecific binding.

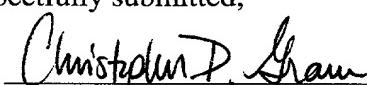
Neither Berenson *et al.* nor Rothschild *et al.* provides the motivation asserted in the Office Action, either explicitly or through knowledge generally attributable to one skilled in the art at the time the invention was made. Thus, the combination of Rasmussen *et al.*, Berenson *et al.* and Rothschild *et al.* is improper and the combination cannot render the present invention obvious under 35 U.S.C. § 103.

Furthermore, even if, *arguendo*, Berenson *et al.* or Rothschild *et al.* did provide the motivation asserted in the Office Action, the rule of *In re Baird*, that a claim to a species within a genus is not rendered obvious and unpatentable by an earlier broad generic disclosure, would still apply. Thus, it would not have been obvious to one skilled in the art at the time the invention was made to combine Rasmussen *et al.* with either or both of Berenson *et al.* and Rothschild *et al.* to arrive at the present invention. Therefore, Applicants submit that claims 12-17 are in condition for allowance.

CONCLUSION

Entry of the foregoing preliminary amendment prior to substantive examination is courteously requested. Examination and allowance of the pending claims is respectfully requested.

Respectfully submitted,

By 
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Version with markings to show changes made

IN THE SPECIFICATION

Paragraph beginning at page 7, line 12:

Other porous azlactone-functional supports are described in PCT Patent Publication WO 93/06925 (Rasmussen et al.) and U.S. Pat. No. 5,993,935 (Rasmussen et al.), issued November 30, 1999 [copending, coassigned, U.S. Pat. Appln. Ser. No. 08/776,601], incorporated herein by reference, in which azlactone-functional particles are incorporated into a continuous porous matrix such as fibrillated polytetrafluoroethylene membrane or a nonwoven web.

IN THE CLAIMS

12. (Amended) An interacted support, comprising:

- (a) an azlactone-functional support,
- (b) a biologically active substance covalently coupled to the support, and
- (c) [a] whole cells interacting with said substance,

wherein the azlactone-functional support comprises one or more base polymer supports that have been prescreened and identified as exhibiting minimal nonspecific binding of the whole cells.

13. (Amended) The support of Claim 12, wherein the azlactone-functional support is a support having a surface comprising azlactone moieties, the support comprising [selected from the group consisting of] a bead, a particulate, a membrane, a blended article, a graft copolymeric article, a woven web, a nonwoven web, a solid plastic particle [having a surface comprising azlactone moieties, and combinations], or any combination thereof.